What is claimed:

1. A method of decreasing intraocular pressure or improving ocular accommodation in an animal, including a human, comprising administering an intraocular pressure decreasing or ocular accommodation improving amount of a compound of the formula I:

Het–Y **(I)**

wherein:

a. Het is a five or six membered heterocycle having a first ring nitrogen and optionally, a second or third ring nitrogen, with the remaining ring atoms being carbon, oxygen, or sulfur; provided that Het is not thiazole, imidazole, oxazole, or dihydro or tetrahydro analogs thereof;

b. Het can be substituted on carbon atoms with

1. one or more substituents independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C_1-C_3)alkylenedioxy, allyl, amino, ω-alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), cycloalkyl, dialkylamino, halo, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylthio, alkylsulfonyl, alkylsulfinyl, alkylsulfonamido, trifluoromethyl, morpholin-4-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, thiomorpholin-4-yl, piperidin-1-yl, Ar* {wherein, consistent with the rules of aromaticity, Ar* is C_6 or C_{10} aryl or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be optionally fused to a substituted benzene, pyridine, pyrimidine, pyridazine, pyrazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Het)}, Ar*–alkyl, Ar*-O, Ar*SO_2-, Ar*SO-, Ar*S-, Ar*SO_2NH-, Ar*NH, (N-Ar*)(N-alkyl)N-, Ar*C(O)-, Ar*C(O)NH-, Ar*NH-C(O)-, and (N-Ar*)(N-alkyl)N-C(O)-; or

2. two adjacent substitutions together with their ring carbons form a fused C_6 or C_{10} aryl ring which aryl ring can be substituted as set forth below; or

3. two adjacent substitutions together with their ring carbons form a C_5-C_7 fused cycloalkyl ring having up to two double bonds including any fused double bond

of the Het group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo; or

4. two adjacent substitutions together with their ring carbons form a fused 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N; or

5. two adjacent substitutions together with their ring carbons form a fused five to eight membered fused heterocycle, wherein the ring fusion is at a carbon-carbon bond of Het, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, sulfur, or $S(O)_n$, wherein S(O)n is 1 or 2; and

c. Het can be substituted on ring nitrogen atoms with

1. hydrogen, alkyl, alkoxycarbonylalkyl-, Ar*, Ar*alkyl-, Ar*C(O)alkyl-, ArS*(O)alkyl-, Ar*$S(O)_2$alkyl-, so long as the ring nitrogen atoms are not quaternized;

2. amino; or

3. at most one nitrogen with oxido (-O^-) to form an N-oxide; and

d. Y is substituted on a ring carbon adjacent to the first or second ring nitrogens and is

1. hydrogen, oxo, alkyl, mercapto, alkylthio, amino, amino(C_1-C_5)alkyl, or aminophenyl, wherein the amino of the latter three groups can be (a) substituted with

(a) Ar^*,

(b) Ar^*-Z-, Ar^*-alkyl-Z-, Ar^*-Z-alkyl-, Ar^*-amino-Z-, Ar^*-aminoalkyl-Z- or Ar^*-oxyalkyl-Z-, wherein Z is a carbonyl or $S(O)_2$ or

(c) formyl or alkanoyl,

2. -$NHC(O)(CH_2)_n$-D-R^eR^f, wherein D is oxygen, sulfur or nitrogen, wherein when D is nitrogen n is 0, 1 or 2, but when D is oxygen or sulfur n=1 or 2, and R^f is present only when D is nitrogen,

wherein

(a) R^e is

(1) Ar^*, or

(2) a group of the formula

Het^{δ}–

wherein Het^{δ} is independently the same as Het, or

(3) a C_3-C_8 cycloalkyl ring having up to one double bond with the proviso that the carbon linking the cycloalkyl ring to D is saturated, which cycloalkyl ring can be substituted by one or more alkyl-, alkoxycarbonyl-, amino-, aminocarbonyl-, carboxy-, fluoro-, or oxo-substituents, or

(4) hydrogen, (C_2-C_6)hydroxyalkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkoxyimino), alkoxycarbonyl, Ar*, or Ar*-alkyl-; and

(b) R^f is independently hydrogen, hydroxy(C_2-C_6)alkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, independently a group Ar* or Ar*-alkyl;

wherein aryl or Ar* in addition to any substitutions specifically noted can be substituted with one or more substituents selected from the group of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C_1-C_3)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω- alkylenesulfonic acid, alkylthio, allyl, amino, Ar*C(O)-, Ar*C(O)NH-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, Ar*O-, Ar*-, Ar*-alkyl-, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, piperidin-1-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, and 4-[C_6 or C_{10}]arylpiperazin-1-yl; and

heterocycles except those of Het or Ar*, can be substituted with, in addition to substitutions specifically noted, one or more substituents selected from acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, Ar*C(O)-, Ar*O-, Ar*-, Ar*-alkyl, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, 4-[C_6 or C_{10}]arylpiperidin-1-yl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, (C_1-C_3)alkylenedioxy, oxo, sulfamoyl, and trifluoromethyl;

or a pharmaceutically acceptable salt of said compounds,

with the proviso that where the compound of formula I is administered to decrease intraocular pressure at least one compound of formula I administered in effective amount is not a triazole, thiadiazole, tetrazole or pyridotriazole substituted on a ring carbon sulfonamide (the amide of which can be substituted) that has carbonic anhydrase inhibiting activity.

2. The method of claim 1, wherein

a. Het is a five or six membered heterocycle having a first ring nitrogen and optionally, a second or third ring nitrogen, with the remaining ring atoms being carbon, oxygen, or sulfur; provided that Het is not thiazole, imidazole, oxazole, or dihydro or tetrahydro analogs thereof;

b. Het can be substituted on carbon atoms with

1. one or more substituents independently selected from hydrogen, acylamino, alkanoyl, alkanoylalkyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, amino, ω- alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), cycloalkyl, dialkylamino, halo, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylthio, alkylsulfonyl, alkylsulfinyl, alkylsulfonamido, trifluoromethyl, morpholin-4-yl, thiomorpholin-4-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, piperidin-1-yl, Ar* {wherein, consistent with the rules of aromaticity, Ar* is C_6 or C_{10} aryl or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be optionally fused to a substituted benzene, pyridine, pyrimidine, pyridazine, pyrazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Het)}, Ar*–alkyl, Ar*-O, Ar*SO_2-, Ar*SO-, Ar*S-, Ar*SO_2NH-, Ar*NH, (N-Ar*)(N-alkyl)N-, Ar*C(O)-, Ar*C(O)NH-, Ar*NH-C(O)-, and (N-Ar*)(N-alkyl)N-C(O)-; or

2. two adjacent substitutions together with their ring carbons form a fused C_6 or C_{10} aryl ring which aryl ring can be substituted as set forth below; or

3. two adjacent substitutions together with their ring carbons form a C_5-C_7 fused cycloalkyl ring having no double bonds except any fused double bond of the Het group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo; and

c. Het can be substituted on ring nitrogen atoms with

1. hydrogen, alkyl, alkoxycarbonylalkyl-, Ar*, Ar*alkyl-, Ar*C(O)alkyl-, ArS*(O)alkyl-, Ar*$S(O)_2$alkyl-, so long as the ring nitrogen atoms are not quaternized;

2. amino; or

3. at most one nitrogen with oxido (-O^-) to form an N-oxide; and

d. Y is substituted on a ring carbon adjacent to the first or second ring nitrogens and is

1. hydrogen, oxo, alkyl, mercapto, alkylthio, amino, amino(C_1-C_5)alkyl, or aminophenyl, wherein the amino of the latter three groups can be (a) substituted with

(a) Ar^*,

(b) Ar^*-Z-, Ar^*-alkyl-Z-, Ar^*-Z-alkyl-, Ar^*-amino-Z-, Ar^*-aminoalkyl-Z- or Ar^*-oxyalkyl-Z-, wherein Z is a carbonyl or $S(O)_2$ or

(c) formyl or alkanoyl,

2. -$NHC(O)(CH_2)_n$-D-R^cR^f, wherein D is oxygen, sulfur or nitrogen, wherein when D is nitrogen n is 0, 1 or 2, but when D is oxygen or sulfur n=1 or 2, and R^f is present only when D is nitrogen,

wherein

(a) R^c is

(1) Ar^*,

(2) a group of the formula

Het^{δ}–

wherein Het^{δ} is independently the same as Het,

(3) a C_3-C_8 cycloalkyl ring having up to one double bond with the proviso that the carbon linking the cycloalkyl ring to D is saturated, which cycloalkyl ring can be substituted by one or more alkyl-, alkoxycarbonyl-, amino-, aminocarbonyl-, carboxy-, fluoro-, or oxo-

substituents, where multiple substituents are located on different carbon atoms of the cycloalkyl ring, except in the case of alkyl, alkoxycarbonyl, and fluoro substituents, which can be located on the same or different carbon atoms; or

(4) hydrogen, (C_2-C_6)hydroxyalkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkoxyimino), alkoxycarbonyl, Ar*, or Ar*-alkyl-; and

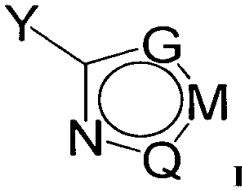
(b) R^f is independently hydrogen, hydroxy(C_2-C_6)alkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, independently a group Ar* or Ar*-alkyl;

wherein aryl or Ar* in addition to any substitutions specifically noted can be substituted with one or more substituents selected from the group of alkyl, amino, dialkylamino, 1-pyrrolidinyl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl; and

heterocycles except those of Het or Ar*, can be substituted with, in addition to substitutions specifically noted, one or more substituents selected from acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, Ar*C(O)-, Ar*O-, Ar*-, Ar*-alkyl, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, 4-[C_6 or C_{10}]arylpiperidin-1-yl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, (C_1-C_3)alkylenedioxy, oxo, sulfamoyl, and trifluoromethyl;

or a pharmaceutically acceptable salt of said compounds.

3. The method of claim 1, wherein Het-Y is



II

wherein G, M, and Q are selected from the group consisting of O, S, C-R^h, C-R^i, and N-R^g, with the proviso that only one of G or Q can be O or S,

a. wherein R^g, is

(1) hydrogen, alkyl, alkoxycarbonylalkyl-, Ar*, Ar*-alkyl-, Ar*C(O)alkyl-, Ar*S(O)alkyl-, or Ar*$S(O)_2$alkyl-, so long as the ring nitrogen atoms are not quaternized; or

(2) amino or oxido (wherein N-R^g forms an N-oxide) and

b. wherein R^h or R^i are

(1) independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C_1-C_3)alkylenedioxy, allyl, amino, ω- alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), cycloalkyl, dialkylamino, halo, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylthio, alkylsulfonyl, alkylsulfinyl, alkylsulfonamido, trifluoromethyl, morpholin-4-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, thiomorpholin-4-yl, piperidin-1-yl, Ar*, Ar*–alkyl, Ar*-O, Ar*SO_2-, Ar*SO-, Ar*S-, Ar*SO_2NH-, Ar*NH, (N-Ar*)(N-alkyl)N-, Ar*C(O)-, Ar*C(O)NH-, Ar*NH-C(O)-, and (N-Ar*)(N-alkyl)N-C(O)-; or;

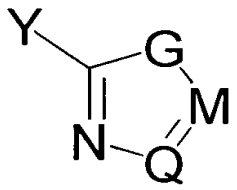
(2) R^h and R^i where adjacent, together with their ring carbons form a C_5-C_7 fused cycloalkyl ring having up to two double bonds including the fused double bond of the Het group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl-, alkoxycarbonyl-, amino-, aminocarbonyl-, carboxy-, fluoro-, or oxo- substituents, except in the case of alkyl, alkoxycarbonyl, and fluoro substituents, which can be located on the same or different carbon atoms;

(3) R^h and R^i where adjacent, together with their ring carbons form a fused C6 or C10 aryl ring;

(4) R^h and R^i where adjacent, together with their ring carbons form a fused five to eight membered fused heterocycle, wherein the ring fusion is at a carbon-carbon bond of Het, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, sulfur, or S(O)n, wherein $S(O)_n$ is 1 or 2; or

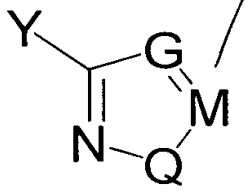
(5) R^h and R^i where adjacent, together with their ring carbons form a fused 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of N for the 6-membered fused heteroaryl rings and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered fused heteroaryl rings.

4. The method of claim 3, wherein Het-Y is



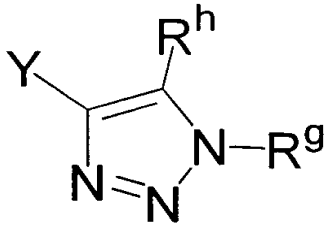
wherein G is O, S, N-R^g;
M is N or C-R^h; or
Q is N or C-R^i.

5. The method of claim 3, wherein Het-Y is

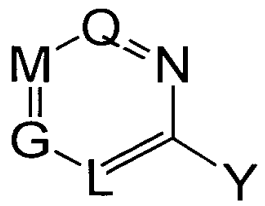


wherein G is N or C-R^h;
M is N or C-R; and
Q is O, S, or N-R^g.

6. The method of claim 3, wherein Het-Y is



7. The method of claim 1, wherein Het-Y is



wherein Q, M, G and L are independently N, C-R^j, C-R^k, C-R^l, or C-R^m, with the proviso that there are 1 to 3 N atoms in the ring, wherein

R^j, R^k, R^l and R^m are

a. independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C_1-C_3)alkylenedioxy, allyl, amino, ω- alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), cycloalkyl, dialkylamino, halo, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylthio, alkylsulfonyl, alkylsulfinyl, alkylsulfonamido, trifluoromethyl, morpholin-4-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, thiomorpholin-4-yl, piperidin-1-yl, Ar*, Ar*–alkyl, Ar*-O, Ar*SO_2-, Ar*SO-, Ar*S-, Ar*SO_2NH-, Ar*NH, (N-Ar*)(N-alkyl)N-, Ar*C(O)-, Ar*C(O)NH-, Ar*NH-C(O)-, and (N-Ar*)(N-alkyl)N-C(O)-; or

b. where two of R^j, R^k, R^l or R^m are adjacent, together with their ring carbons form a C_5-C_7 fused cycloalkyl ring having up to two double bonds including the fused double bond of the Het group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl-, alkoxycarbonyl-, amino-, aminocarbonyl-, carboxy-, fluoro-, or oxo- substituents, wherein multiple substituents are located on different carbon atoms of the cycloalkyl ring, except in the case of alkyl, alkoxycarbonyl, and fluoro substituents, which may be located on the same or different carbon atoms; or

c. where two of R^j, R^k, R^l and R^m are adjacent, together with their ring carbons form a fused C6 or C10 aryl; or

d. where two of R^j, R^k, R^l and R^m are adjacent, together with their ring carbons form a fused five to eight membered fused heterocycle, wherein the ring fusion is at a

carbon-carbon bond of Het, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, sulfur, or $S(O)_n$, wherein n is 1 or 2; or

e. where two of R^j, R^k, R^l and R^m are adjacent, together with their ring carbons form a fused 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of N for the 6-membered fused heteroaryl rings and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered fused heteroaryl rings.

8. The method of claim 7,

a. wherein L is N;

b. G is C-R^j;

c. M is C-R^k;

d. Q is C-R^l; and

e. Y is amino, amino(C_1-C_5)alkyl, or aminophenyl, wherein the amino of all three groups can be substituted with

(1) Ar^*,

(2) Ar^*-Z-, Ar^*-alkyl-Z-, Ar^*-Z-alkyl-, Ar^*-amino-Z-, Ar^*-aminoalkyl-Z- or Ar^*-oxyalkyl-Z-, wherein Z is a carbonyl or $S(O)_2$ or

(3) formyl or alkanoyl.

9. The method of claim 7,

a. wherein L and Q are N;

b. G is C-R^j;

c. M is C-R^k; and

d. Y is amino, amino(C_1-C_5)alkyl, or aminophenyl, wherein the amino of all three groups can be substituted with

(1) Ar^*,

(2) Ar^*-Z-, Ar^*-alkyl-Z-, Ar^*-Z-alkyl-, Ar^*-amino-Z-, Ar^*-aminoalkyl-Z- or Ar^*-oxyalkyl-Z-, wherein Z is a carbonyl or $S(O)_2$ or

(3) formyl or alkanoyl.

10. The method of claim 3,

a. wherein Q is N;

b. G is N-R^g;

c. M is C-R^h; and

d. Y is amino, amino(C_1-C_5)alkyl, or aminophenyl, wherein the amino of all three groups can be substituted with

(1) Ar^*,

(2) Ar^*-Z-, Ar^*-alkyl-Z-, Ar^*-Z-alkyl-, Ar^*-amino-Z-, Ar^*-aminoalkyl-Z- or Ar^*-oxyalkyl-Z-, wherein Z is a carbonyl or $S(O)_2$ or

(3) formyl or alkanoyl.